EXHIBIT 1

Curriculum vitae

Name: Yasumichi Hitoshi, MD. Ph.D.

Born: November 21, 1961. Kumamoto, Japan

Citizenship: Japan

Present Position: Associate director, Project leader

Present address: Department of Cell Biology
Rigel pharmaceutical Inc.,
240 East grand avenue,
CA 94081
U.S. A.
Telephone: 650-624-1128
Facsimile: 650-624-1101
E-mail: yhitoshi@rigel.com

Professional experience:

2002.7-present Associate director, Project leader

Department of Department of Cell Biology,

Rigel pharmaceutical Inc.

Research:

2002.1-2002.7 Group leader, Project leader

Department of Department of Cell Biology,

Rigel pharmaceutical Inc.

Research:

1998.12-2001.12 Senior scientist, Project leader

Department of Department of Cell Biology,

Rigel pharmaceutical Inc.

Research: Identification of proteins and peptides that play an important role in cell cycle regulation of specific tumor cells using retroviral functional screens.

1998.2-1998.12 Senior scientist
Department of Department of Cell Biology,
Rigel pharmaceutical Inc.
Research: Characterization of a membrane receptor, Toso, which inhibit TNF receptor family-induced apoptosis.

1995.3-1998.2 Postdoctoral Fellow
Department of Molecular Pharmacology, Stanford University.
Research: Analysis of signaling pathway using high titer retrovirus.
Scientific Advisor: Assistant Professor Garry P. Nolan

1992.1-1995.3 Postgraduate Research Associate
Department of Immunology,
The Institute of Medical Science,
The University of Tokyo.
Scientific Advisor: Professor Kiyoshi Takatsu
Research: Cellular mechanism of development of a retrovirus-induced immunodeficiency syndrome (MAIDS)

1991.4-1991.12 Postgraduate Research Associate
Department of Biology,
The Institute for Medical Immunology,
Kumamoto University Medical School.
Scientific Advisor: Professor Kiyoshi Takatsu
Research: Signal transduction through IL-5 receptor and involvement of Xid defect in the receptor system.

Education:

Medical School

1981-1987 Kumamoto University Medical School

Graduate School

1987-1991 Department of Biology,
The Institute for Medical Science,
Kumamoto University Medical School
Research: Immunology
Scientific Advisor: Professor Kiyoshi Takatsu

Thesis Dissertation: Role of interleukin 5 and its receptor in the immune system.

Membership of learned societies:

Japanese Society of Immunology
Japanese Cancer Association

Honors and Fellowships

Special Fellow of The Japanese Ministry of Education, Culture and Science, April 1990-March 1991.

The Uehara Memorial Foundation Fellowship, April 1995-March 1996.

Publications

1. Mita, S., Harada, N., Naomi, S., **Hitoshi, Y.**, Sakamoto, K., Akagi, M., Tominaga, A. & Takatsu, K., (**1988**). Receptors for T cell-replacing factor / Interleukin 5 Specificity, quantitation, and its implication. J. Exp. Med., 168, 863 - 878.

2. Jankovic, D.L., Abehsira-Amar, O., Korner, M., Roth, C., **Hitoshi, Y.**, Takatsu, K. & Theze, J., (**1988**). IL-4, but not IL-5, can act synergistically with B cell activating factor (BCAF) to induce proliferation of resting B cells. Cell. Immunol., 117, 165 - 176.

3. **Hitoshi, Y.**, Mita, S., Tominaga, A., Kikuchi, Y., Sonoda, E., Takatsu, K. & Watanabe, Y., (**1989**). Interferon-gamma inhibits the proliferation but not the differentiation of murine B cells in response to IL-5. Int. Immunol., 1, 185 - 190.

4. Tominaga, A., Mita, S., Kikuchi, Y., **Hitoshi, Y.**, Takatsu, K., Nishikawa, S.-I. & Ogawa, M., (**1989**). Establishment of IL-5-dependent early B cell lines by long-term bone marrow cultures. Growth Factors, 1, 135 - 146.

5. Matsumoto, R., Matsumoto, M., Mita, S., **Hitoshi, Y.**, Ando, M., Araki, S., Yamaguchi, N., Tominaga, A. & Takatsu, K., (**1989**). Interleukin-5 induces maturation but not class switching of surface IgA-positive B cells into IgA-secreting cells. Immunology, 66, 32 - 38.

6. Sonoda, E., Matsumoto, R., **Hitoshi, Y.**, Ishii, T., Sugimoto, M., Araki, S., Tominaga, A., Yamaguchi, N. & Takatsu, K., (**1989**). Transforming growth factor β induces IgA production and acts additively with interleukin 5 for IgA production. J. Exp. Med., 170, 1415 - 1420.

7. Mita, S., Tominaga, A., **Hitoshi, Y.**, Sakamoto, K., Honjo, T., Akagi, M., Kikuchi, Y., Yamaguchi, N. & Takatsu, K., (**1989**). Characterization of high-affinity receptors for interleukin 5 on interleukin 5-dependent cell lines. Proc. Natl. Acad. Sci. USA, 86, 2311 - 2315.

8. Enokihara, H., Furusawa, S., Nakakubo, H., Kajitani, H., Nagashima, S., Saito, K., Shishido, H., **Hitoshi, Y.**, Takatsu, K., Noma, T., Shimizu, A. & Honjo, T., (**1989**). T cells from eosinophilic patient produce interleukin-5 with interleukin-2 stimulation. Blood, 73, 1809 - 1813.

9. Takaki, S., Tominaga, A., **Hitoshi, Y.**, Mita, S., Sonoda, E., Yamaguchi, N. & Takatsu, K., (**1990**). Molecular cloning and expression of the murine interleukin-5 receptor. EMBO J., 9, 4367-4374.

10. Murata, Y., Yamaguchi, N., **Hitoshi, Y.**, Tominaga, A. & Takatsu, K., (**1990**). Interleukin 5 and interleukin 3 induce serine and tyrosine phosphorylation of several cellular proteins in an interleukin 5-dependent cell line. Biochem. Biophys. Res. Commun., 173, 1102-1108.

11. Mita, S., Kikuchi, Y., **Hitoshi, Y.**, Sakamoto, K., Tominaga, A. & Takatsu, K., (**1990**). Cyclosporin A preferentially inhibits the differentiation of murine B cells in response to IL-5 and its restoration by IL-6. Kumamoto Med. J., 42, 73-86.

12. **Hitoshi, Y.**, Yamaguchi, N., Mita, S., Sonoda, E., Takaki, S., Tominaga, A. & Takatsu, K., (**1990**). Distribution of IL-5 receptor-positive B cells : Expression of IL-5 receptor on Ly-1(CD5)$^+$ B cells. J. Immunol., 144, 4218 - 4225.

13. Enokihara, H., Kajitani, H., Nagashima, S., Tsunogake, S., Takano, N., Saitou, K., Furusawa, S., Shishido, H., **Hitoshi, Y.** & Takatsu, K., (**1990**). Interleukin 5 activity in sera from patients with eosinophilia. Brit. J. Haematol., 75, 458 - 462.

14. Yamaguchi, Y., Suda, T., Shiozaki, H., Miura, Y., **Hitoshi, Y.**, Tominaga, A., Takatsu, K. & Kasahara, T., (**1990**). Role of IL-5 in IL-2-induced eosinophilia In vivo and in vitro expression of IL-5 mRNA by IL-2. J. Immunol., 145, 873 - 877.

15. Yamaguchi, N., **Hitoshi, Y.**, Mita, S., Hosoya, Y., Murata, Y., Kikuchi, Y., Tominaga, A. & Takatsu, K., (**1990**). Characterization of the murine interleukin 5 receptor by using a monoclonal antibody. Int. Immunol., 2, 181 - 187.

16. Yamaguchi, Y., Suda, T., Suda, J., Eguchi, M., Miura, Y., Mita, S., **Hitoshi, Y.**, Tominaga, A. & Takatsu, K., (**1990**). Analysis of eosinophil-predominant colonies formed by human hemopoietic precursor cells in the presence of purified interleukin-5. Acta Haematol. Jpn, 53, 688 - 698.

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23. Sonoda, E., **Hitoshi, Y.**, Yamaguchi, N., Ishii, T., Tominaga, A., Araki, S. & Takatsu, K., (**1992**). Differential Regulation of IgA Production by TGF-β and IL-5: TGF-β induces Surface IgA-Positive Cells Bearing IL-5 Receptor, Whereas IL-5 Promotes Their Survival and Maturation into IgA-Secreting Cells. Cell. Immunology, 140, 158-172.

24. **Hitoshi, Y.**, Okada, Y., Sonoda, E., Tominaga, A., Makino, M., Suzuki, K., Kinoshita, J., Komuro, K., Mizuochi, T. & Takatsu, K., (**1993**). Delayed progression of a murine retrovirus-induced acquired immunodeficiency syndrome, MAIDS, in X-linked immunodeficient mice. J. Exp. Med., 177, 621-626.

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29. Miyake, K., Yamashita, Y., **Hitoshi, Y.**, Takatsu, K. & Kimoto, M., (**1994**). Murine B cell Proliferation and Protection from Apoptosis with an Antibody against a 105-kD Molecule: Unresponsiveness of X-linked Immunodeficient B Cells. J. Exp. Med., 180, 1217-1224.

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32. Korenaga, M., **Hitoshi, Y.**, Takatsu, K. & Tada, I., (**1994**). Regulatory effect of anti-interleukin 5 monoclonal antibody on intestinal worm burden in a primary infection with Strongyloides Venezuelensis in mice. Int. J. Parasitology, 24, 951-957.

33. Korenaga, M., **Hitoshi, Y.**, Takatsu, K. & Tada, I., (**1995**). Cross-resistance between Strongyloides vebezuelensis and S. ratti in mice. J. Helminthology, 69, 119-123.

34. Makino, M., Yoshimatsu, K., Azuma, M., Okada, Y., **Hitoshi, Y.**, Yagita, H., Takatsu, K., & Komuro, K., (**1995**). Rapid development of murine AIDS is dependent of signals provided by CD54 and CD11a. J. Immunol., 155, 974-981.

35. Numata, F., **Hitoshi, Y.**, Uehara, S., & Takatsu, K. (**1997**). The xid mutation plays an important role in delayed development of murine acquired immunodeficiency syndrome. Int. Immunol., 9, 139-46.

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37. Rothenberg, M., Fisher, J., Zapol, D., Anderson, D., **Hitoshi, Y.**, Achacoso, P., and Nolan, G.P., (**1998**) Intracellular combinatorial chemistry with peptides in selection of Caspase-like inhibitors. NATO ASI Series, Vol. H 105:171-183. Gene Therapy.

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40. Perez, O. D., Kioshita, S., **Hitoshi, Y.**, Payan D. G., Kitamura T., Nolan, G. P., & Lorens J. B., (**2002**). Activation of the PKB/AKT pathway by ICAM2. Immunity, 1, 51-65

Patent

1. Toso, a cell-surface specific regulator of Fas-induced apoptosis in T cells
   Stanford Docket S98-019

Atty Dkt. No.: RICE012
USSN: 09/509,196

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.
Typed or Printed Name Steven Goldstein
Signature [signature] Date 2/5/03

#24
D.9.1
2/13/03

DECLARATION OF YASUMICHI HITOSHI UNDER 37 C.F.R. § 1.132 Address to: Assistant Commissioner for Patents Washington, D.C. 20231	Attorney Docket Confirmation No.	RICE-012 8868
	First Named Inventor	Roger John Daly
	Application Number	09/509,196
	Filing Date	March 23, 2000
	Group Art Unit	1646
	Examiner Name	Olga N. Chernyshev
	Title	"Potential Effector for the GRB7 Family of Signalling Proteins"

Dear Sir:

1. I, Yasumichi Hitoshi, M.D., Ph.D. declare and say I am a resident of the U.S.A. My residence address is 331 Callippe Court, Brisbane, CA 94005.

2. I hold a M.D. degree, which I received from Kumamoto University Medical School in 1987. I further hold a Ph.D. degree which I received from Kumamoto University Medical School in 1991. I am an expert in the fields of oncology research, retroviral technology, and cell cycle regulation. A copy of my curriculum vitae is attached as Exhibit 1.

3. I am currently hold the position of Associate Director at Rigel Pharmaceuticals, Inc.

4. I have read both the specificationof U.S. patent application serial no. 09/509,196 (the '196 application) and the Office Action dated November 5, 2002 issued by the Examinerin this same patent application.

5. I understand that the pending claims are directed to a polynucleotide encoding the protein 2.2412, which is now referred to in the literature as Tankyrase2 or TaHo (Tankyrase Homolog), as well as vectors and host cells containing this polynucleotide, and use of this polynucleotide to produce the encoded 2.2412 protein.

6. I understand that the Patent Office has rejected all pending claims on the basis that the utility asserted in the '196 application is not credible. I further understand that the asserted utility disputed by the Patent Office is the use of 2.2412-encoding polynucleotide or 2.2412 protein as a tumor marker.

Review of the '196 Application

7. The '196 application sets out the following statements (page and line numbers in brackets refer to the specific parts of the '196 application::

a) **2.2412 protein is an effector protein for the Grb7 family of signalling proteins** (a protein that specifically binds to a signaling protein to facilitate a signal transduction cascade)
   i) **2.2412 protein specifically binds Grb14 and specifically binds Grb7** (page 10, line 26 to page 11, line 32)
   ii) **binding of 2.2412 protein to Grb14 requires the N-terminal region of Grb14, which contains highly conserved proline-rich motif thought to mediates interaction of the Grb7 family of proteins with their effectors** (page 11, lines 29-32)
   iii) **2.2412 contains multiple ankyrin repeats, which are known to have a role in protein-protein interactions** (page 9, lines 25-34)

b) **Grb7 family members are signal transduction molecules that exhibit differential expression in certain human cancers (particularly breast cancer)** (page 5, lines 13-15). Specifically, at the time of filing

i) Grb7 family members were known to be associated with oesophageal carcinoma,[1] primary gastric cancer,[2] and breast cancer.[3]

ii) **Grb14 was known to be differentially expressed in breast cancer**[4]

iii) **Grb7 was known to be differentially expressed in breast cancer**[5]

8. Given that 2.2412 specifically binds Grb14 and specifically binds Grb7, each which were known at the time the application was filed (September 23, 1997) to be differentially expressed in cancer cells compared to normal cells, it is reasonable to conclude that effectors for these proteins such as 2.2412 will also be differentially expressed (specification page 5, lines 13-16).

9. In my opinion, the '196 application sets out a credible association of 2.2412 expression and human cancers.

10. This association of 2.2412 expression with human cancers has been further supported in at least two publications. Specifically, 2.2412 (also known as Tankyrase2[6]) has been reported to be a tumor-specific antigen as evidenced by detection of anti-Tankyerase2 antibodies in sera of breast cancer patients[7] and in sera of patients having meningioma.[8]

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[1] Tanaka et al. 1997 Cancer Res. 57:28-31.
[2] Kishi et al. 1997 Biochem Biophys. Res. Commn. 232:5-9.
[3] Stein et al. 1994 EMBO J 13:1331-40.
[4] Daly et al. 1996 J. Biol. Chem 271:12502-10.
[5] Stein et al. 1994 EMBO J 13:1331-40
[6] Lyons et al. 2001 J. Biol. Chem. 276:17172-80.
[7] Kuimov et al., 2001 Genes Immun. 2:52-5.
[8] Monz et al., 2001 Clin. Cancer Res. 7:113-9.

11. In summary, after reviewing the '196 application, it is my opinion that a person having ordinary skill reading the '196 application at the time the application was filed (September 23, 1997) would find the assertion that 2.2412 (Tankyrase2) is a tumor marker to be credible in view of the disclosure in the specification as set out above.

Additional Data Confirming the Use of 2.2412 as a Tumor Marker

12. In my position at Rigel Pharmaceuticals, Inc., I have directed others and personally performed research to examine the expression of 2.2412 (also referred to as Tankyrase2 or Tankyrase Homologue (TaHo)) in both normal and cancerous human cells.

13. Expression of 2.2412 was examined using a Taqman Assay. Matched tumor and normal cDNAs from lung and breast tissue were obtained from two different sources: BioChain Inc. and Clontech (clinical histories of Clontech cDNAs were not available). Location of the primers within the 2.2412 (TaHo) sequence are indicated as bolded and underlined sequences in Exhibit 2. In addition, the TaHo sequence was aligned with the Tankyrase sequence in order to demonstrate the specificity of the Taqman analysis using these primers for Tankyrase homologue. Analysis was done in triplicate and standard errors for normal and tumor tissue were determined. Expression levels in the matched samples were normalized to Ribosomal Protein S9 (S9) and the 23kD Highly Basic Protein (HBP).

14. The results of these studies are shown in Exhibit 3. As shown in the graphs, 2.2412 is expressed at significantly higher levels in two types of lung cancer (bronchioalveolar carcinoma and large cell carcinoma) relative to normal lung tissue. 2.2412 is also expressed at significantly higher levels in three types of breast cancer (invasive ductal carcinoma, intraductal carcinoma and invasive lobular carcinoma) compare to normal breast tissue.

15. These data further support the assertion in the '196 application that the 2.2412 protein and its encoding polynucleotide are useful as a tumor marker.

16. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such will false statements may jeopardize the validity of the application or any patent issuing thereon.

2/3/03
Date

Yasumichi Hitoshi, Ph.D.

Attachments:

Exhibit 1: Curriculum vitae of Dr. Yasumichi Hitoshi
Exhibit 2: Primers used in expression analysis of 2.2412
Exhibit 3: Graphs showing expression of 2.2412 in normal and cancerous human cells

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